



Robert Greene Sterne  
Jorge A. Goldstein  
David K.S. Cornwell  
Robert W. Esmond  
Tracy-Gene G. Durkin  
Michele A. Cimbalà  
Michael B. Ray  
Robert E. Sokohl  
Eric K. Steffe  
Michael Q. Lee  
Steven R. Ludwig  
John M. Covert  
Linda E. Horner  
Robert C. Millonig  
Donald J. Featherstone  
Timothy J. Shea, Jr  
Michael V. Messenger  
Judith U. Kim

Patrick E. Garrett  
Jeffrey T. Helvey  
Heidi L. Kraus  
Eldora L. Ellison  
Thomas C. Fiala  
Donald R. Banowitz  
Peter A. Jackman  
Jeffrey S. Weaver  
Brian J. Del Buono  
Edward W. Yee  
Vincent L. Capuano  
Virgil Lee Beaton  
Theodore A. Wood  
Elizabeth J. Haanes  
Joseph S. Ostroff  
Frank R. Cottingham  
Rae Lynn P. Guest  
Daniel A. Klein

Jason D. Eisenberg  
Michael D. Specht  
Tracy L. Muller  
Jon E. Wright  
LuAnne M. DeSantis  
Ann E. Summerfield  
Helene C. Carlson  
Cynthia M. Bouchez  
Timothy A. Doyle  
Gabby L. Longworth  
Lori A. Gordon  
Laura A. Vogel  
Bryan S. Wade  
Bashir M.S. Ali  
Shannon A. Carroll  
Matthew E. Kelley  
Michelle K. Holoubek  
Marsha A. Rose

Christopher J. Walsh  
W. Blake Coblenz  
James J. Pohl\*  
Young Tang  
John T. Haran\*  
Mark W. Rygiel

**Registered Patent Agents\***  
Karen R. Markowicz  
Matthew J. Dowd  
Katrina Yujian Pei Quach  
Bryan L. Skelton  
Robert A. Schwartzman  
Victoria S. Rutherford  
Simon J. Elliott  
Julie A. Heider  
Mita Mukherjee  
Scott M. Woodhouse

Liliana Di Nola-Baron  
Peter A. Socarras  
Jeffrey K. Mills  
Danielle Letting  
Lori Branges

**Of Counsel**  
Edward J. Kessler  
Kenneth C. Bass III  
Marvin C. Guthrie

\*Admitted only in Maryland  
\*Admitted only in Virginia  
\*Practice Limited to  
Federal Agencies

IFW \$CU

September 22, 2006

**WRITER'S DIRECT NUMBER:**  
(202) 772-8834  
**INTERNET ADDRESS:**  
BHAANES@SKGF.COM

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**Art Unit 1633**

**Attn: Mail Stop Amendment**

Re: U.S. Utility Patent Application  
Application No. 10/618,299; Filed: July 11, 2003  
For: **Method of Enhancing Delivery of a Therapeutic Nucleic Acid**  
Inventors: Barsoum *et al.*  
Our Ref: 2159.0830001/EJH/SAS

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Credit Card Payment Form (PTO-2038) in the amount of \$180.00 to cover the Information Disclosure Statement fee;
2. First Supplemental Information Disclosure Statement;
3. One (1) page of Form PTO/SB/08A citing two (2) documents (US1-US2);
4. Two (2) pages of Form PTO/SB/08B citing eighteen (18) documents (NPL1-NPL18);
5. Copies of eighteen (18) cited documents (NPL1-NPL18); and
6. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

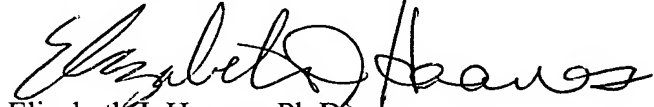
8

Commissioner for Patents  
September 22, 2006  
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in black ink, appearing to read "Elizabeth Haanes", written over the printed name.

Elizabeth J. Haanes, Ph.D.  
Attorney for Applicants  
Registration No. 42,613

EJH/SAS:dms  
Enclosures



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Barsoum *et al.*

Appl. No.: 10/618,299

Filed: July 11, 2003

For: **Method of Enhancing Delivery of a  
Therapeutic Nucleic Acid**

Confirmation No.: 6907

Art Unit: 1633

Examiner: Robert M. Kelly

Atty. Docket: 2159.0830001/EJH/SAS

**First Supplemental Information Disclosure Statement  
Under 37 C.F.R. § 1.97(c)**

*Mail Stop Amendment*

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying IDS Forms, PTO/SB/08A and PTO/SB/08B, are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98.

Copies of documents **NPL1** to **NPL18** are submitted. However, in accordance with 37 C.F.R. § 1.98(a)(2), copies of U.S. patents and patent application publications, **US1** to **US2**, cited on the attached IDS Form, PTO/SB/08A, are not submitted.

The Examiner's attention is directed to the related issued Patent No. 6,696,423 (Document **US1**) and the following co-pending U.S. Patent Application, which is directed to related technical subject matter:

Application No. 10/395,712, inventors James G. Barsoum, *et al.*, filed March 20, 2003; published on December 11, 2003 as U.S. Publication No 2003/0229042 A1 (Document **US2**).

09/25/2006 MBERHE 00000020 10618299

01 FC:1806

180.00 0P

The identification of this U.S. Patent Application is not to be construed as a waiver of secrecy as to that application now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited application and the art cited therein during examination.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached IDS Forms based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed more than three months after the U.S. filing date and after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection, or Notice of Allowance, or an

action that otherwise closes prosecution in the application. Attached is out PTO-2038 Credit Card Payment Form in the amount of \$180.00 in payment of the fee under 37 C.F.R. § 1.17(p).

It is respectfully requested that the Examiner initial and return a copy of the enclosed IDS Forms, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

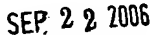


Elizabeth J. Haanes, Ph.D.  
Attorney for Applicants  
Registration No. 42,613

Date: Sept. 22, 2006

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600

584605v1



Approved for use through 09/30/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

**FIRST SUPPLEMENTAL  
INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**  
*(Use as many sheets as necessary)*

U.S. PATENT DOCUMENTS

## FOREIGN PATENT DOCUMENTS

76

Examiner  
Signature

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

*If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.*



PTO/SB/08B (07-06)

Approved for use through 09/30/2006. OMB 0651-0031  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use as many sheets as necessary)		<b>Complete if Known</b>			
		Application Number	10/618,299		
		Filing Date	July 11, 2003		
		First Named Inventor	James G. Barsoum		
		Art Unit	1633		
		Examiner Name	Robert M. Kelly		
Sheet	1	of	2	Attorney Docket Number	2159.0830001/EJH/SAS

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	NPL1	Brunner, K.T., <i>et al.</i> , "Blood Clearance of P <sub>32</sub> -Labeled Vesicular Stomatitis and NewCastle Disease Viruses by the Reticuloendothelial System in Mice," <i>J. Immunol.</i> , 85:99-105, American Association of Immunologists (1960)	
	NPL2	Cai, P., <i>et al.</i> , "Methyl palmitate: Inhibitor of phagocytosis in primary rat Kupffer cells," <i>Toxicol.</i> 210:197-204, Elsevier Ireland Ltd. (June 2005)	
	NPL3	Dachs, G.U., <i>et al.</i> , "Targeting Gene Therapy to Cancer: a Review," <i>Oncol. Res.</i> 9:313-325, Cognizant Communication Corporation (1997)	
	NPL4	Fahimi, H.D., "The Fine Structural Localization of Endogenous and Exogenous Peroxidase Activity in Kupffer Cells of Rat Liver," <i>J. Cell Biol.</i> 47:247-262, Rockefeller University Press (1970)	
	NPL5	Kirn, A., <i>et al.</i> , "Uptake of Viruses by Kupffer Cells Isolated from Human Liver," <i>Lancet North Am. Ed.</i> 2:585-586, Lancet Publishing Group (1980)	
	NPL6	Kolb-Bachofen, V., "Uptake of Toxic Silica Particles by Isolated Rat Liver Macrophages (Kupffer Cells) Is Receptor Mediated and Can Be Blocked by Competition," <i>J. Clin. Invest.</i> 90:1819-1824, The American Society for Clinical Investigation, Inc. (1992)	
	NPL7	Laurent, N., <i>et al.</i> , "Uptake by rat liver and intracellular fate of plasmid DNA complexed with poly-L-lysine or poly-D-lysine," <i>FEBS Lett.</i> 443:61-65, Federation of European Biochemical Societies (1999)	
	NPL8	Kuzmin, A.I., <i>et al.</i> , "Macrophage depletion increases the safety, efficacy and persistence of adenovirus-mediated gene transfer in vivo," <i>Gene Ther.</i> 4:309-316, Stockton Press (1997)	
	NPL9	Marianneau, P., <i>et al.</i> , "Infection of Primary Cultures of Human Kupffer Cells by Dengue Virus: No Viral Progeny Synthesis, but Cytokine Production Is Evident," <i>J. Virol.</i> 73:5201-5206, American Society for Microbiology (1999)	
	NPL10	McCuskey, R.S., <i>et al.</i> , "Kupffer Cell Function in Host Defense," <i>Rev. Infect. Dis.</i> 9:S616-S619, The University of Chicago (1987)	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO  <b>FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>				<b>Complete if Known</b>	
				Application Number	10/618,299
				Filing Date	July 11, 2003
				First Named Inventor	James G. Barsoum
				Art Unit	1633
				Examiner Name	Robert M. Kelly
Sheet	2	of	2	Attorney Docket Number	2159.0830001/EJH/SAS

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume number, publisher, city and/or country where published	T <sup>2</sup>
	NPL11	Miller, N., and Vile, R., "Targeted vectors for gene therapy," <i>FASEB J.</i> 9:190-199, The Federation of American Societies for Experimental Biology (1995)	
	NPL12	Mogensen, S.C., "Macrophages and Age-Dependent Resistance to Hepatitis Induced by Herpes Simplex Virus Type 2 in Mice," <i>Infect. Immun.</i> 19:46-50, American Society for Microbiology (1978)	
	NPL13	Rentsch, M., <i>et al.</i> , "Benefit of Kupffer cell modulation with glycine versus Kupffer cell depletion after liver transplantation in the rat: effects on postischemic reperfusion injury, apoptotic cell death graft regeneration and survival," <i>Transpl. Int.</i> 18:1079-1089, European Society for Organ Transplantation (September 2005)	
	NPL14	Rubin, D.H., <i>et al.</i> , "Transport of Infectious Reovirus into Bile: Class II Major Histocompatibility Antigen-Bearing Cells Determine Reovirus Transport," <i>J. Virol</i> 61:3222-3226, American Society for Microbiology (1987)	
	NPL15	Selgrade, M.K., and Osborn, J.E., "Role of Macrophages in Resistance to Murine Cytomegalovirus," <i>Infect. Immun.</i> 10:1383-1390, American Society for Microbiology (1974)	
	NPL16	van Til, N.P., <i>et al.</i> , "Kupffer Cells and Not Liver Sinusoidal Endothelial Cells Prevent Lentiviral Transduction of Hepatocytes," <i>Mol. Ther.</i> 11:26-34, The American Society of Gene Therapy (January 2005)	
	NPL17	Wake, K., <i>et al.</i> , "Cell Biology and Kinetics of Kupffer Cells in the Liver," <i>Int. Rev. Cytol.</i> 118:173-229, Academic Press, Inc. (1989)	
	NPL18	Zenilman, M.E., <i>et al.</i> , "Use of Ricin A-Chain to Selectively Deplete Kupffer Cells," <i>J. Surg. Res.</i> 45:82-89, Academic Press, Inc. (1988)	

582847v1

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.